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KDIGO Controversies Conference on Coronary Artery & Valvular Diseases in Chronic Kidney Disease

**June 28 - July 1, 2018
Vienna, Austria**

Kidney Disease: Improving Global Outcomes (KDIGO) is an international organization whose mission is to improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines. Periodically, KDIGO hosts conferences on topics of importance to patients with kidney disease. These conferences are designed to review the state of the art on a focused subject and to ask conference participants to determine what needs to be done in this area to improve patient care and outcomes. Sometimes the recommendations from these conferences lead to KDIGO guideline efforts and other times they highlight areas for which additional research is needed to produce evidence that might lead to guidelines in the future. The current Controversies Conference is the third in a series related to cardiovascular disease (CVD) and kidney disease sponsored by KDIGO. The first dealt with management of arrhythmias in chronic kidney disease (CKD) and the second, management of heart failure in CKD.

Background

CVD is the leading cause of morbidity and mortality in patients with CKD. The increased risk of CVD begins during the earlier stages of CKD before the onset of kidney failure. Patients with CKD have a high prevalence of traditional coronary artery disease (CAD) risk factors such as diabetes and hypertension but they are also exposed to other non-traditional, uremia-related CVD risk factors such as inflammation, oxidative stress and abnormal calcium-phosphorus metabolism. Mitral annular calcification and aortic calcification are also highly prevalent in CKD and lead to conduction system abnormalities, endocarditis, embolism, as well as valvular stenosis and regurgitation.

Relevance of the Conference and Topic

Coronary artery disease and valvular disease are leading causes of hospitalizations in most developed countries and CKD is a major risk factor for both these conditions. The prevalence of CKD is expected



to increase in the future because of its close relationship to diabetes, hypertension and obesity. Data from the general population cannot be extrapolated to CKD because the pathophysiology of the CVD in CKD is different, the prevalence of comorbid conditions in CKD is high, and the potential side effects of interventions in CKD are higher still. We therefore need a better understanding of the epidemiology of CAD and valvular disease in CKD. We also need an improved appreciation of the pathophysiology, diagnosis, and treatment of CAD and valvular disease in CKD.

Conference Overview

The conference will be led by Mark J. Sarnak MD MS, nephrologist from Tufts Medical Center, Boston USA and Thomas H. Marwick, MBBS, PhD, MPH, cardiologist from Baker Heart and Diabetes Institute, Melbourne, Australia. This interactive conference will invite key thought leaders from cardiology, nephrology, cardiac surgery and other related disciplines who will comprehensively review the literature, and summarize what is known and what is not known in this field. Key areas of controversy will be focused upon and research and clinical recommendations will be provided so as to move the field forward. There will be four breakout groups that will focus on CKD and dialysis patients and one breakout group that will focus on kidney transplant recipients (see table below).

	Population	Focus
Breakout Group 1	CKD and Dialysis	Epidemiology & Screening of CAD and Valvular Disease
Breakout Group 2	CKD and Dialysis	Pathology & Pathophysiology of CAD and Valvular Disease
Breakout Group 3	CKD and Dialysis	Diagnosis & Treatment of Prevalent CAD
Breakout Group 4	CKD and Dialysis	Diagnosis & Treatment of Prevalent Valvular Disease
Breakout Group 5	Transplant	CAD and Valvular Disease in Kidney Transplant Recipients



APPENDIX: SCOPE OF COVERAGE

GROUP 1: EPIDEMIOLOGY AND SCREENING OF CAD AND VALVULAR DISEASE IN CKD AND DIALYSIS PATIENTS

Epidemiology and risk prediction of CAD

1. Does the presentation of CAD differ across the spectrum of CKD (from CKD, through CKD-D and CKD-T)?
2. Are standard ASCVD risk equations accurate in patients with CKD/ESKD/Transplant?
3. Is there any evidence that conventional risk markers (e.g. hypertension, diabetes) affect ASCVD risk differently in patients with CKD/ESKD/Transplant?

Screening for CAD

4. When, how often and with what methods should the risk of CAD be assessed in CKD/ESKD?

Valvular heart disease

5. Does the presentation of valvular disease across the spectrum of CKD (from CKD, through CKD-D and CKD-T)?
6. Is the incidence of valvular heart disease affected by CKD/ESKD?
7. Should patients with CKD/ESKD be screened for valvular disease?

GROUP 2: PATHOLOGY AND PATHOPHYSIOLOGY OF CAD AND VALVULAR DISEASE IN CKD AND DIALYSIS PATIENTS

PATHOLOGY

1. Pathology of CAD and valvular disease
 - a. What are the specific pathological characteristics of CAD and valvular heart disease in CKD patients (e.g., coronary media calcification, severity of disease and others)? How do these



- characteristics modify the course of the disease or specifically add to the increased risk (i.e., plaque rupture)?
- b. What role does the cause of CKD play?
 - c. Clinical presentation at different stages of CKD What are potential implications for assessment and treatment of CAD in CKD?
2. Differences in comparison with the general population
 - a. What are the main cardiovascular risks at different stages of CKD compared to the general population?
 - b. Are there differences in the outcomes of cardiovascular complications in CKD versus the general population due to these differences in pathology? (e.g., myocardial infarction in CKD compared to the general population?)

PATHOPHYSIOLOGY

3. Atherosclerosis
 - a. Dyslipidemia: What is the impact of CKD on lipid abnormalities? Impact of dyslipidemia on atherosclerosis mechanism in CKD?
 - b. Inflammation and oxidative stress: What impact does CKD have on inflammation and oxidative stress and in turn, on atherosclerosis?
 - c. What is the impact of CKD on plaque vulnerability?
4. Arteriosclerosis
 - a. What are the roles of mineral and bone disease (MBD), blood pressure, inflammation and hemodynamic factors in the development of arteriosclerosis?
 - b. What is the role of coronary microcirculation for cardiovascular risk in CKD?
5. Plaque vulnerability
6. Calcification
 - a. Prognostic significance in the absence of hemodynamic disturbance
 - b. What does the role of mineral bone disease (MBD) play in the pathology of coronary and valvular heart disease in CKD (e.g., in plaque and media calcification)? What are the potential therapeutic implications and effects on cardiovascular risk?
 - c. Arterial stiffness: What is the role of arterial stiffness on left ventricular hypertrophy in CKD?
 - d. Arterial calcification: What is the role of calcification in arterial stiffness and plaque stability?



7. Dialysis as a trigger for ischemia
 - a. Effect of arteriovenous fistula
 - b. Anemia
 - c. Electrolytes disorders during HD sessions
 - d. Choice of modality relative to underlying CAD, e.g., myocardial stunning and ultrafiltration rate
 - e. Reducing intra-dialytic hypotension – by reducing UFR, hemodiafiltration, Changing dialysate Ca, using cold dialysis temp in patients with established underlying CAD?

GROUP 3: DIAGNOSIS AND TREATMENT OF PREVALENT CAD IN CKD AND DIALYSIS PATIENTS

DIAGNOSIS OF CAD

1. What is the preferred test for the diagnosis of prevalent CAD in individuals with CKD and ESKD?
 - a. Functional - Exercise stress testing without imaging vs stress imaging (exercise or pharmacological) e.g., echocardiography, SPECT, PET, MRI (non-gadolinium based)
 - b. Is there a role for CT scan determination of coronary artery calcification (CAC)? Should the Agatston CAC score or the volume-based CAC score be used for the assessment of calcium deposits?
 - c. Anatomic - coronary CTA, catheterization – avoidance of contrast induced nephropathy/AKI
2. Use of troponins in the diagnosis of CAD in CKD/ESKD and differences from the general population.

PRESENTATION OF CAD

3. Difference in manifestations (signs and symptoms of CAD);
 - a. between CKD vs ESRD vs controls?
 - b. peritoneal dialysis and hemodialysis?
 - c. Men vs. women or children vs. adults in each of these subtypes of dialysis?
 - d. Role of home nocturnal HD vs. in-center HD (e.g., do calcification effects alter signs and symptoms/pathophysiology)?



- e. Intradialytic myocardial stunning?

TREATMENT OF CAD

4. Are standard guideline-directed medical therapies for prevention of CAD effective in patients with CKD?
 - a. Should CKD/ESKD be considered a CAD equivalent
 - b. How should patients with CKD/ESKD and CAD be treated with lipid-lowering therapies? (e.g., statins, ezetimibe plus statin or other lipid-lowering strategies?)
 - c. Should there be a LDL treatment target in CKD and ESKD? Any role for non-statin medical therapies?
 - d. Comparative effectiveness of primary/secondary ACS prevention and therapies.
 - e. Risks and benefits of various anticoagulation strategies in acute coronary syndromes

REVASCULARIZATION

5. Are the indications for revascularization therapy in CKD different when compared with patients in whom kidney function is preserved? (e.g., elective for chronic CAD vs acute for ACS?)
6. Is the risk of AKI and progression to ESKD a reason to withhold angiography and revascularization in otherwise suitable patients with CKD/ESKD? (e.g., PCI, CABG)
7. Access sites for PCI; Risks and benefits of radial access in patients with CKD/ESKD
8. Should multi-vessel CAD or high-risk CAD be preferentially treated with PCI in place of CABG in CKD or ESKD patients? (e.g., CABG vs PCI for left main CAD) Would treatment approach differ in patients with CKD vs. those being treated with dialysis?
9. What measures should be taken to reduce the risk of AKI in patients undergoing revascularization (e.g., PCI, CABG)?
10. Should duration of dual antiplatelet therapy be shortened in CKD patients?



GROUP 4: DIAGNOSIS AND TREATMENT OF PREVALENT VALVULAR DISEASE IN CKD AND DIALYSIS PATIENTS

Epidemiology

1. What are the morbidity and mortality rates for interventions in aortic stenosis (AS): TAVI vs., AVR vs., AVR + root? Compared to the general population?
2. What are the morbidity and mortality rates for interventions mitral valve disease: repair vs., MVR? Compared to the general population?

Mechanisms of Valvular Disease

3. What are the types and mechanisms of valvular disease and how do these differ in CKD/ESKD versus the general population? Specifically address the question of mitral annular calcification in ESKD and can this entity cause severe mitral stenosis?
4. Prevalence of pulmonary HTN and right sided valvular dysfunction in ESKD: etiology and management
5. Effect of arteriovenous fistula

Diagnosis of Valvular Disease (Including hemodynamic assessment)

6. How do we evaluate valve disease [aortic stenosis (AS)/aortic regurgitation/mitral stenosis/mitral regurgitation/ tricuspid valve disease (TR)] in the general population and are there differences that should be considered in CKD and ESKD?
7. How to evaluate patients with mixed (i.e., MR+MS) or combined valvular heart disease? (MR and TR) or MR and AS, etc
8. In dialysis patients, is it important at what time in the dialysis cycle assessments are done?



Treatment of Valvular Disease

9. What are treatments of choice for patients with CKD and ESKD with valvular disease?
 - a. Medical therapy: What are the medical therapies for valvular disease and are there any differences in the general population versus CKD/ESKD?
 - b. Anticoagulation: Should anticoagulation (yes/no) and/or targets be the same for CKD non-dialysis, PD and HD patients? If not, what should they be? How should anticoagulation be monitored? Should monitoring change when a non-dialysis CKD patient progresses to become more uremic (where bleeding risk is greater?)
 - c. Non-operative: What are the non-operative valve interventions for valvular disease including TAVR, mitral clip, mitral balloon valvuloplasty, tricuspid interventions and are there any differences in CKD/ESKD from the general population?
 - d. Surgical: What are the surgical therapies for valvular disease and are there differences in CKD/ESKD from the general population? Implications of early bioprosthetic valve degeneration on prosthesis selection, timing of therapy and medical therapy. What strategies should be used to prevent AKI and its sequelae during valve replacement surgery?
 - e. Transcatheter valve replacement (TAVR):
 - i. Challenges in patient selection (clinical and anatomical) – strategies to minimize contrast utilization
 - ii. Prosthesis durability
 - iii. Complications (pacemaker, endocarditis, etc)

Endocarditis

10. What is the optimal diagnostic and therapeutic management for endocarditis in CKD/ESKD? Endocarditis at each valve position and address subacute bacterial endocarditis prophylaxis as well as treatment approaches with antibiotics alone (AV or MV endocarditis in ESKD ever treatable alone with antibiotics?) and with surgery (case fatality rates with surgery).



GROUP 5: CAD AND VALVULAR DISEASE IN KIDNEY TRANSPLANT RECIPIENTS

Pre-operative screening for CAD

1. What are the objectives of screening for CAD prior to transplantation? Should pre-transplant patients be evaluated for CAD? If so, with what test(s)?
2. Which patient groups should be screened for CAD prior to transplantation?
 - a. Should cardiac work-up for pre-transplant evaluation in high CVD risk (e.g., diabetes) be different from non-high risk
 - b. Should the approach to perioperative screening differ in deceased versus living donor candidates?
3. How frequently should there be further evaluation for CAD in patients with a normal stress test awaiting kidney transplant?
4. What tools and research are needed to enable prediction of atherosclerotic plaque rupture in the perioperative period?

Pre-operative management to mitigate peri-op CV risk

5. Which patients should be revascularized prior to transplantation?
 - a. Which patients are candidates for percutaneous revascularization and which patients should be treated with coronary artery by-pass grafting?
6. What non-surgical therapies should be used to reduce perioperative CAD events?

Post-operative risk

7. How does risk of delayed graft function modify post-operative risk?
8. How should patients be risk stratified after transplantation?
9. With regard to post-transplant risk, do we need to identify novel risk factors or should we simply treat patients with established risk factors better?



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Valvular disease

10. What valvular disease is clinically relevant and when should it be treated in kidney transplantation candidates?

11. Should transplant patients be screened for valvular disease?